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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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DISEASES of the NERVOUS SYSTEM

(PUBLISHED MONTHLY)

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

*Guide to the Indications for Brain Wave Recording**

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The electroencephalogram is of outstanding value in neurological and psychiatric disorders because it provides the examining physician with a direct estimate of the brain's activity—accomplished by a procedure that is neither painful nor prejudicial to the patient. The prospective value of a brain wave recording is more often predictable by correct interpretation of symptoms than by a collection of positive signs pointing to the existence of a neurologic condition. It is not a substitute for the neurologic examination; rather it is a special phase of it, as are lumbar puncture and pneumoencephalography, offering the prospect of diagnosis when other neurological findings are absent. Electroencephalography may bring to light evidence of a lesion hidden in a "silent area," or otherwise too concealed to give clinical signs.

The neuropsychiatrist is often called upon to clarify the first manifestations of convulsions, headache, vertigo, visual or speech disturbance, amnesia or personality disorder. He may be puzzled by the diversity of implications that attach to the presenting symptoms. When objective evidence for the existence of a disease process is wanting, he is fortunate to have available a technique which aids in separating objectively the organic from the functional. It is my purpose to survey the clinical situations in which the electroencephalogram has a definite value in establishing the correct diagnosis. Conditions are also indicated in which records of brain activity are likely to provide information that is useful but not necessarily vital to diagnosis.

The primary purpose is accomplished by presenting selected case briefs each illustrating a recurring diagnostic problem in which a record of brain activity may be expected to have importance either in diagnosis or in determining the course of treatment. Unless otherwise stated the usual neurological examination was non-contributory in each case used for illustration. The secondary purpose is achieved by relating the electroencephalographic findings in a variety of neurological conditions. The material used in the survey was drawn from a series of several thousand cases in which both adequate histories and the results of electroencephalography were available. This is supplemented by comments on observations of others.

The historical (Davis[1]) and technical (Gibbs & Gibbs[2]) aspects of electroencephalography are covered elsewhere. Emphasis herein is placed upon the symptomatic approach to the indications for brain wave recording. The recordings were classified by the Gibbs (Gibbs, Gibbs & Lennox[3]) method, but to avoid technical language they are referred to here as *fast, slow* and *paroxysmally* disordered. Where a focal neurological diagnosis was made with the aid of electroencephalography, the part of the hemisphere is noted over which the abnormality was recorded.

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The Convulsive States

When convulsive spells repeat at intervals, it is not difficult to make the clinical diagnosis of epilepsy; it is usually possible to classify the pattern as grand mal, petit mal, psychomotor, or mixed type. The chief value of the brain wave recording lies in aiding to establish the etiology of seizures, and in providing the cue to diagnosis when they are infrequent, of very recent origin, atypical, or appear as substitute phenomena for convulsions.

1. *The First Convulsion*

One of the troublesome problems in convulsive states is establishing an undoubted diagnosis in the child, adolescent or adult who has had one, or a few, widely spaced convulsive seizures. Not infrequently such a seizure may be nocturnal; it may follow a period of overwork, or change in diet or in environment. It may be precipitated by emotional factors. In any case it is usually poorly described by the apprehensive relatives. The occurrence of the first seizure in an adult may forecast the diagnosis of brain tumor or other serious organic brain involvement.

Case 1: A girl aged 7 had a previous nocturnal attack at the age of 4. A recent convulsion, also nocturnal, was right-sided. An electroencephalogram taken a few days thereafter showed a resting pattern that was definitely slow. This was interrupted by a paroxysmal sequence that appeared to arise in the *left* temporal region establishing the focal origin of the convulsive pattern. Prior to taking the brain wave record the two convulsions were considered to have occurred on a hypoglycemic basis; the positive tracing led to immediate use of anti-convulsant treatment.

Case 2: An adolescent male had his first generalized convulsion at the age of 16. The first brain wave tracing was done soon thereafter, and showed much disordered activity but no focal abnormality. A second record obtained six months later was definitely slow. Both records were consistent with the existence of convulsive disorder. The patient was placed on Dilantin medication after the first seizure because of the degree of abnormality evident in the record, and there was no repetition of the attack. Had the record of brain activity after the first attack been normal or equivocal, anti-convulsant medication would have been delayed pending the occurrence of another seizure.

Case 3: An adult male, age 28, had his first convulsive attack in 1945. Within one month he commenced to show personality changes, and become notably slow in performance. He then had a second seizure. When examined he showed a partial expressive aphasia, gait disturbance and neurological findings relating to the right side of the body. An electroencephalogram showed a disordered record of slow type with a focus of high voltage slow waves over the left fronto-temporal region of the brain. At operation an oligodendroglioma was removed from that site. In this case the brain wave tracing detected a focal abnormality in brain activity which related to the clinical signs and suggested the site of pathology.

2. *Cases Presenting Confusion between Convulsive Episodes and Syncope*

The electroencephalogram is also indicated when there are recurring brief episodes of unconsciousness that give the appearance of being syncopal in character. Often these do not present definitive evidence that one is dealing with convulsive seizures until some change in the character of the attack suggests an epileptic basis.

Case 4: A 33 year old male examined in 1945 gave a history of fainting spells occurring twice monthly since September 1942. The spells usually occurred without warning but some were preceded by dizziness and nausea. On occasions a true loss of consciousness did not occur; in spells of the latter character he was stuporous for a brief period following which there was residual confusion lasting for several hours. The brain wave recording showed a definite slow abnormality which was considered highly consistent with a diagnosis of convulsive disorder. Before it was obtained the spells were interpreted as attacks of simple syncope.

3. *Petit Mal and Partial Seizures*

The brain wave tracing also has an important advantage in aiding in the distinction between petit mal and partial seizures. Petit mal attacks present a 5 to 10 seconds loss of consciousness without aura, and motor phenomena are usually restricted to upward movement of the eyeballs, and sometimes haphazard movements of the hands. In partial seizures a convulsion of brief duration may appear in and spread from a part of the body (one foot, hand, or side of the face) without loss of consciousness (Jacksonian seizures); or there is an oft-repeated aura (such as a peculiar odor or a flash of light), suggesting involvement of a particular sensory field. The attack may occur without loss of consciousness. Such partial seizures may be noted in an individual who also has grand

mal seizures that are ushered in by the happenings of the partial seizure; in that case the convulsive basis of the partial seizures is readily recognized. However, partial seizures can occur without there being a history of grand mal attacks and with trivial if any loss of consciousness; frequently this leads to confusion with petit mal attacks. It is important to differentiate between partial and petit mal seizures, for Tridione is in our experience the most effective anticonvulsant medication for petit mal, whereas hydantoin derivatives such as Dilantin and Mesantoin are more effective medical remedies in partial seizures. The brain wave recording may be of considerable discriminating value, since 3 per second repeating wave and spike electrical disturbances may be recorded from all lead combinations in petit mal cases; on the other hand, partial seizures frequently show focal disturbances of pattern that relate to the area of cerebral cortex where presumption on clinical grounds would indicate that the attack should originate.

Surgically the differentiation between petit mal and partial seizure patterns also has marked significance, since petit mal seizures give a generalized disturbance not indicative of a surgical condition, whereas partial seizures may relate to a phase in the slow development of an expanding brain lesion. Examples giving the character of partial seizures, and the results of brain wave recordings follow.

Case 5: A 26 year old male gave a fourteen month history of brief spells each initiated by an aura of formless flashes of light "in front of the right eye" that moved in from a distance. When they became close he "lost control of himself," and did not remember his actions later. During one such spell he was noted to speak distinctly but irrationally. In other such spells he was noted to flex his arms and fall, but there was no obvious loss of consciousness. He recalls an auto accident that preceded an attack; he did not see an auto approaching on the right side. Visual fields showed a partial right hemianopsia. Pneumoencephalogram was within normal limits except for a difference in position between the posterior horns of the lateral ventricles. Electroencephalogram showed a left occipital slow spike focus.

Case 6: For the past eighteen months a 38 year old male had complained of spells lasting for about one minute each. During observed attacks he rose from bed, walked a few steps turned with an expression of rage, gritting his teeth and clenching his fists. Thereafter he returned to bed and regained consciousness. He had complete amnesia for these spells. On other occasions while at home he had acted peculiarly for brief periods, had walked into things, and once burned himself with a cigarette. There was a focally disordered pattern in the left temporal area which appeared on hyperventilation. Pneumoencephalogram was normal. Spinal fluid protein on several occasions was over 100 milligrams per cent.

4. *Change in Character of the Seizure Pattern*

When generalized convulsive seizures have occurred over a number of years, and the attacks change to discrete Jacksonian type, the situation should not be met complacently. The new pattern may indicate the development of space taking pathology.

Case 7: A 31 year old white female gave a history of frequent generalized convulsive seizures from childhood to age 28. There were two significant head traumata at ages 10 and 27. At the age of 31, after complete absence of seizures for two years, she commenced to note occasional twitching in her left hand which lasted one or two minutes and occasionally involved the left leg as well. No loss of consciousness accompanied the Jacksonian attacks. Her brain activity pattern was diffusely disordered but contained sporadic slow waves arising from the right frontal area. At craniotomy a protoplasmic astrocytoma was removed from the right premotor area.

5. *Comment*

In addition to its usefulness in aiding to establish the etiology of a convulsive condition, the brain wave tracing has considerable value in determining the probability of success once medical treatment is undertaken. We find that those subjects with convulsive disorder who present very disordered slow, fast, or pace irregularity records respond less readily to anti-convulsants and the physician may experience considerable difficulty in bringing such cases under complete medical control. On the other hand, when the record taken in the interim between seizures is normal or only mildly abnormal, we feel that more encouragement can be given that attacks can be abolished, provided proper anticonvulsant medication can be chosen. It is important in the treatment of convulsive disorder that the early choice of the proper drugs in sufficient dosage leads to decreased frequency of seizures, and thereby increases

the confidence of the patient in the physician. As the inter-seizure intervals lengthen, the patient becomes increasingly determined to accept the way of life previously pointed out by the physician as a prophylactic against further seizures. Thus the medical treatment is effectively complemented by personality adjustment.

The Convulsive Equivalents

Convulsive equivalents are headaches of brief duration, vertiginous attacks, periodic attacks of paroxysmal abdominal pain, brief departures from the pattern of socially acceptable behavior during which there is amnesia, and periods in which there is acceptable performance of routine daily work activity but for which there also may be absence of recollection. The latter two conditions are representative of the type of attack known as the *psychomotor seizure*. Such paroxysmal occurrences as the above are readily fitted into the convulsive disorders when the same individual has true seizures as well but form a puzzling problem when no history of convulsive phenomena can be obtained.

1. *Headache.*

Headaches of this type are of sudden onset, brief duration and paroxysmal occurrence. The quite short duration may arouse suspicion that they are not migrainous in character. There is no amnesia, nor loss of consciousness. The headache may be succeeded by a period of drowsiness such as often follows true convulsive attacks. Headaches that are equivalent phenomena may respond well to proper choice of anti-convulsant medication and be resistant to all other therapeutic procedures.

Case 8: A 23 year old female had periodic brief headaches, without preceding aura, which she characterized as unbearable. The headaches were of too short duration to be considered typical of migraine and did not respond to the conventional treatment for migraine. Brain wave recording revealed a definitely fast pattern. It was considered consistent with a convulsive basis for the headache although definite paroxysmal features were absent. She was placed on Dilantin, grs. one and one-half t.i.d., and the headaches were considerably improved within two weeks.

2. *Vertiginous Episodes.*

Vertigo is the subjective sensation of rotation, either of the individual or of his environment. Its cause may lie in the labyrinth, cerebello-pontine angle, brain stem or cerebral cortex.[4] Occurring paroxysmally, it may precede a genuine convulsion as its aura; or, more rarely, it appears as an entire equivalent for an epileptic attack. It is in these latter manifestations that an abnormal electroencephalogram may have considerable diagnostic value. Since vertigo also may occur in association with migraine, or as an equivalent of a migraine attack, a problem in differential diagnosis between an epileptic and a migranous basis may be presented.

Case 9: A 51 year old man experienced his first attack of severe vertigo one year prior to entry into the hospital. The attacks recurred at bimonthly intervals throughout the year. After each he was drowsy and slept for a few hours. Electroencephalogram showed a moderately slow abnormality. He was placed on Dilantin Sodium, gr. 0.1 t.i.d. The vertiginous attacks were not relieved and he was changed to Tridione, another anti-convulsant. Shortly after being placed on this drug the attacks were abolished.

Visceral Equivalents.

The experience of Penfield and Ericksen[5] indicates that exclusively autonomic seizures without somatic or psychic involvement are rare. Various visceral manifestations occurring either as the aura of seizures or as associated phenomena are much more common. A case in which paroxysmal episodes of recurring acute abdominal pain were the equivalent for seizures has been reported.[6] We have no brain wave recordings on undoubted visceral equivalents for epileptic seizures.

4. *Amnesias.*

Lennox[7] has provided a detailed discussion of amnesia, emphasizing the amnesic components of certain convulsive attacks which he designates as *psychomotor*. It should be noted that not uncommonly a convulsive seizure may be followed by an interval of amnesia during which automatic acts may be performed; and amnesia itself can be a convulsive equivalent. In our experience amnesic equivalents may take one of several forms: A period during which customary activities are attended to, the person recovering to recognize that he has no recollection for elapsed time, although he may have tangible proof of his activities in the way of notes taken or work accomplished. Or, during

the amnesic period, the person may wander about aimlessly, or in a state of automatism, and perform actions or sequences of actions that tend to repeat at each attack. On account of their extended duration certain amnesias which last weeks or more and do not conform to the pattern of hysterical amnesia are difficult to explain. Neither are they easily accounted for on an epileptic basis unless they represent extended post-convulsive sequelae of undetected seizures.

Case 10: A 20 year old female had a history of the occurrence of spells of "faintness" during childhood. Relatives described her as "pampered and high tempered." Prior to hospitalization she had an amnesic episode that lasted for several days. On admission she was experiencing an attack thought to be hysterical blindness, and during it an epileptiform seizure occurred also described as hysterical. Brain wave recording showed a definitely disordered record interrupted by sporadic paroxysmal sequences. In this case the amnesic episode may well have occurred subsequent to an unwitnessed epileptic attack.

5. *Automatic Activity Equivalents.*

We recognize the necessity for careful examination of claims that actions indicative of criminal intent were performed without recollection by the subject. The gain to the perpetrator of criminal acts in avoiding responsibility is great; and Lennox remarks that a physician is more apt to be given a reliable history than is a court of law. In the interest of justice there is grave reluctance to accept the view that the perpetrator of a crime is not responsible for his act. Yet acts that are apparently impulsive in character are sometimes carried out during an amnesic period as the equivalent of an epileptic seizure. In such cases the electroencephalogram may provide useful information in distinguishing a true epileptic equivalent from a feigned amnesia for a criminal act.

Case 11: A male, age 24, had a reliable history of two skull fractures during childhood. He was of superior intelligence, but had episodes of impulsive stealing and destructive behavior for which amnesia was claimed. His brain wave record was unusually fast and repeatedly showed evidences of paroxysmal activity.

Migraine

In the convulsive states records of the brain's activity that are taken during interseizure intervals are frequently a valuable diagnostic adjunct. There is insufficient evidence to recommend the procedure similarly for those susceptible to episodes of migraine. Recordings performed in the intervals between migraine headaches are frequently normal. When disordered brain wave patterns are obtained in migraine cases they may be evident as paroxysmal activity, by the unusually fast nature of the record, or by a difference in recorded voltage between corresponding pairs of electrodes on the two sides of the head.

If the record is obtained at the onset of a headache, which infrequently happens except in research studies, information may be obtained that is useful in explaining the patho-physiology of the process causing migraine. Random slow waves may occur in a left or right-sided lead combination suggesting an associated transient disturbance of cerebral function.

It is not always easy to distinguish between the common headache of migraine and the rare headache that presents as an epileptic equivalent unless the electroencephalogram gives outstanding evidence of disordered activity suggestive of a convulsive basis. It may be necessary to resort to trial periods of medication to distinguish between the two. Paroxysmal vertigo may be a migrainous as well as an epileptic equivalent, and it is also necessary to distinguish between "abdominal epilepsy" and "abdominal migraine."

Post-Traumatic States

Following significant cerebral concussion the pattern of brain activity may become slow and diffusely disorganized, the severity and duration of the change being, in general, proportionate to the seriousness of the head injury. If the concussion is mild the changes may quickly disappear (thirty minutes) (Dow, Ulett and Raaf[7]). Commonly such post-concussion alteration in the record will be gone within several weeks following the head injury. When brain contusion complicates concussion, focal slow abnormalities in pattern (that appear to be related to the site of contusion) may be detected on a background of less disordered activity. Acute and chronic subdural hematomas while not yielding a specific pattern of disordered activity may also show related focal abnormality.

As delayed sequelae to head injury epileptic seizures may occur. It may happen that the

head injury to which the onset of seizures is attributed is trivial. In these cases suspicion should be aroused that the disorder apparent in the brain's activity pre-existed the injury. When the head trauma has been severe, the expectancy of residual abnormality in the brain's activity is substantially increased. And the occurrence of focal fast or slow patterns related to the site of a head injury, or understandable in terms of predictable remote effects of a blow, would appear to bear causal relation to post-traumatic convulsive seizures.

An abnormal wave tracing may also aid in establishing the organic basis for a post-traumatic headache (Busse[8]). However, even when there is a recognizable skull defect and post-traumatic headache is the principal complaint, the brain wave tracing may be normal.

Cerebral Neoplasms

Cerebral gliomas that expand beneath the cerebral cortex commonly cause very slow activity to replace the usual brain wave pattern in the region of their growth. Such slow wave sequences are not specific for gliomas since they may also occur at the margins of cerebral cortex rendered ischaemic through vascular occlusion. However, the abnormal activity signalizes the existence of underlying disturbance; and correct interpretation of the cause of the disturbance may be apparent from the chronology of the development of symptoms.

Parasaggital meningiomas sometimes produce focal slow patterns like those noted for subcortical tumors. On the other hand, focal abnormality recorded from their neighborhood may be mild, or altogether missing.

Since the patterns of activity recorded in the electroencephalogram arise in the cerebral hemisphere, the procedure cannot be recommended as a diagnostic aid in cerebellar tumor.

Other Neuropsychiatric Disorders

A variety of conditions that may disrupt the ordered activity of cerebral centers produce changes, sometimes prominent ones, in the brain wave record. The residuals of encephalitis and of meningitis, senile and presenile change, cerebral arteriosclerosis, Huntington's chorea, Wilson's disease and neurosyphilis may cause alterations in the form of the record. Primary metabolic disorders that affect the nervous system secondarily may also alter the pattern of activity. In our experience all such changes are variable and non-specific. They have their chief value in suggesting organic basis for presenting symptoms when other objective evidence for derangement of cerebral function is lacking. Functional psychiatric disorders do not show consistent accompanying alterations in brain activity, and brain wave examinations can only be recommended for their aid in ruling out co-existing organic cerebral involvement in puzzling cases.

Discussion and Summary

The procedure of brain wave recording is a reliable adjunct to the neurological examination. It is of particular value when the symptomatology points to disordered cerebral function, and the usual neurological study has given negative results. This is usually true in paroxysmal disorders of which convulsive conditions, in their more rare as well as in their more common manifestations, form by far the largest group. It is not argued that the electroencephalogram always provides evidence of disordered brain activity in convulsive states. Definite clinical evidence of convulsive disorder may exist and the single brain wave recording, usually obtained during an inter-seizure interval, provide no evidence thereof. When such normal records occur, the individual usually has infrequent seizures and should respond well to anti-convulsant medication when this is deemed necessary. On the other hand, it is believed that a definitely disordered record, obtained after even a single seizure has occurred, suggests that more attacks will follow if medication is not instituted. In individuals who have had more numerous seizures the amount of disorder apparent in the record frequently relates to the difficulty that will be experienced in establishing anti-convulsant control.

The brain wave recording is particularly useful in detecting equivalents for the epileptic seizure which masquerade as symptoms readily attributable to a functional neuropsychiatric condition. A correct diagnosis in the case of convulsive equivalents has much importance since the symptoms are then subject to treatment by anti-convulsants.

Convulsive equivalents mentioned are headache, vertigo, autonomic attacks, certain amnesias and certain manifestations of automatic impulsive activity for which amnesia may also exist. When symptoms of a neuropsychiatric disorder have a convulsive equivalent basis they are resistant to psychiatric therapy alone, although, of course, psychotherapy plays an important—though secondary—role in the medical care of convulsive states.

In migraine, also a paroxysmal disorder, the electroencephalogram provides some useful information concerning the physiologic alterations that usher in the attack. The brain wave recording is not believed necessary for the diagnosis of migraine.

It is noted that the electroencephalogram has a use in assessing the seriousness of cerebral concussion and it has considerable value in post-traumatic epilepsy, the onset of which may occur several years after the head trauma.

The brain wave recording is an excellent diagnostic adjunct when the existence of a cerebral tumor is suspected. Then, focal abnormalities detected over the site of the tumor, usually slow in character, may lead to pneumo-encephalography or ventriculography to verify the diagnosis. When, as may occasionally happen, these direct diagnostic procedures give negative results and suspicion of tumor still exists, the case may be followed with serial brain wave recordings made at intervals of one to three months to detect evidence of increasing abnormality.

Focal softening due to vascular occlusion, and other local disease processes of the cerebral hemisphere may produce focal disorders of the brain wave record, when other neurological evidence of involvement is wanting. Senile arteriosclerotic, and primary degenerative disorders affecting the cerebral hemisphere may also produce their trace of disorganized activity which can be recognized in the electroencephalogram. All such conditions produce non-specific alterations, and the diagnostic value of the test lies in verifying the suspicion that the symptoms in the particular case are organic in character.

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Use of Delvinal Sodium Vinobarbital in the Treatment of Serial Seizures and Status Epilepticus

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Two of the authors (Davidoff and Doolittle) have previously reported on the use of Delvinal Sodium Vinobarbital in epileptic states. It was observed that this drug exercised a favorable effect on psychomotor seizures and on the psychic phenomena which epileptic patients frequently exhibited. Improvement in mental status and diminution of post-convulsive confusion was noted in approximately three quarters of the patients including those who experienced serial seizures.

During the course of the investigation, it was observed that Delvinal Sodium given orally was effective in diminishing the number of serial seizures which the patients experienced during a given period and in aborting the frequency of occurrence of serial seizures in some cases if given early enough in the course of the convulsive manifestation, i.e., at the onset.

In addition, Delvinal Sodium possesses the properties of rapid action and relatively low toxicity. Therefore, as was to be expected, preliminary studies begun in 1943, indicated that intravenous and intramuscular injections of Delvinal Sodium were superior to oral administration of the drug in controlling serial seizures or status epilepticus and in preventing the mental sequalae. At that time intravenous injection of Delvinal Sodium (0.3 G or 5 grains) resulted in almost immediate cessation of status epilepticus in 3 cases. During the course of these investigations intramuscular injection of (0.6 G or 10 grains) of Delvinal Sodium was found to be effective in aborting or terminating serial seizures in 2 cases. (E.T.D.).

Therefore, in this paper, we discuss the results of intravenous and intramuscular injection of Delvinal Sodium in 25 cases with serial seizures and status epilepticus. Twelve cases manifested serial seizures and 13 cases exhibited status epilepticus.

The method of procedure and results are presented in the 20 illustrative abstracts summarized in the case reports. These include 10 consecutive cases of serial seizures and an equal number of consecutive cases of status epilepticus. All these patients were closely observed in the hospital or infirmary wards at Craig Colony. They all were patients at the Colony and resided either in cottages or dormitories. They were transferred to the hospital or infirmary treatment units for close observation where they received Delvinal Sodium after status or serial seizures had developed.

The other 5 cases not included in the consecutive case reports are mentioned in the discussion of the results. Three of these suffered from status epilepticus and two from prolonged serial seizures.

The routine measures which many of the patients previously received to combat serial seizures and status were (1) S.S. enema. (2) 30-120 grains of a triple bromide mixture administered orally or by rectum. (3) Chloral hydrate 10-20 grains was frequently used in combination with the bromide mixture. (4) Phenobarbital sodium (0.3 to 1.0 G) intramuscularly. Chloroform by inhalation was frequently given if these measures failed.

If these medications were ineffectual, previous to this study, sodium amytal (1 G or 15 grains) was injected intravenously. At times sodium amytal was administered without the preliminary routine procedures. In this study, Delvinal Sodium was used frequently after other procedures had failed.

CASE REPORTS

A. *Intravenous Administration*

I. *Serial Seizures*

Case 1: A.R., female, age 19, I.Q. 78
Classification, Idiopathic
Onset of Epilepsy, 6 years
Predominant type of seizure, Grand Mal and Petit Mal (mixed)

Physical Status, Normal; weight 130 lbs.

This patient was admitted to Colony Hospital from cottage dormitory at Craig Colony on July 25, 1946 at 9:50 a. m. because of serial seizures of 6 hours duration. There were 20 grand mal seizures from 9:50 a. m. to 10:30 a. m. The routine measures employed at the cottage to control these seizures had proven ineffectual.

At 10:30 a. m. Delvinal Sodium (0.3 G) was injected intravenously. Four grand mal seizures occurred following this. At 10:50 a. m. the patient again received 0.3 G Sodium Delvinal intravenously. No seizures were noted following the latter injection.

Patient showed no mental or physical sequalae and was returned to her cottage after a 10-day observation period.

Case 2: M.L., male, age 9, I.Q. 15
Classification, Symptomatic - Agenesis
Onset of Epilepsy, 5 months of age
Predominant type of seizure, Grand Mal
Physical Status, Flaccid paralysis and hypotonia of lower extremities. Weight 35 lbs.; emaciated.

This patient was admitted to the hospital on August 27, 1946 at 11:50 a. m. She manifested rapid repeated seizures every 5 minutes since 7:00 a. m. At 13:15 p. m. Delvinal Sodium (0.3 G) was injected intravenously. Seizures ceased until 1:00 p. m. Following this she had 6 grand mal seizures up to 7:20 p. m. Grand mal seizures were manifested at 8:30 p. m. and 9:00 p. m. and 3 more grand mal seizures were observed until 11:00 p. m. Delvinal Sodium (0.3 G) was given intravenously. Seizures ceased while the needle was still in vein and no further convulsive manifestations were evident.

While pulmonary edema is present in most serial seizures of this severity, this phenomenon did not develop in Case 1 or Case 2 after Delvinal Sodium despite the great number of repeated seizures. This patient was discharged to her ward in good condition after a 7-day period of observation.

Case 3: E.H., male, age 32, I.Q. 65
Classification, Idiopathic - Undifferentiated
Onset of Epilepsy, 11 years of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Deformity of left foot and ankle. Weight 140 lbs.

Patient was admitted to hospital on September 4, 1946 at 11:00 a. m. Patient had 8 grand mal seizures from 8:30 a. m. to 11:00 a. m. At 11:00 a. m. he was given Delvinal Sodium (0.6 G) intravenously. Seizures stopped while needle was still in vein. No further seizures nor mental sequalae were noted following administration of Delvinal Sodium. Patient was returned to cottage within 3 days.

Case 4: R.P., male, age 18, I.Q. 78
Classification, Idiopathic
Predominant type of seizure, Grand Mal
Onset of Epilepsy, 3 years of age
Physical Status, Chest rachitic. Weight 85 lbs. This patient was admitted to the hospital on June 26, 1946 with diagnosis of lung abscess.

On September 30, 1946 he had a series of 11 grand mal seizures from 9:30 a. m. to 10:15 a. m. Sodium luminal (0.3 G) given intramuscularly was ineffectual. At 11:15 a. m. Sodium Delvinal (0.3 G) was administered intravenously. Medication was effectual until 9:00 p. m. He then had 4 mild grand mal seizures. He was given 0.3 G of Sodium Delvinal intramuscularly at about 10:00 p. m. No further seizures were observed.

He was discharged from the hospital on December 21, 1946. He had no further serial seizures nor mental sequalae during his residence in the hospital.

Case 5: V.S., male, age 26, I.Q. 30
Classification, Endocrinopathic
Onset of Epilepsy, 8 years of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Upper incisors wide spaced, pegged and notched. Right testicle undescended and about 1/6 normal size. Left testicle small and slid back and forth into scrotum.

He was admitted to hospital on December 3, 1946 at 9:00 a. m. Patient had 5 grand mal seizures from 8:00 a. m. to 9:00 a. m. He was given sodium luminal (0.6 G) intramuscularly at 9:00 a. m. which was ineffectual. He had a grand mal seizure after medication. He was given Delvinal Sodium (0.3 G) intravenously at 10:15 a. m. Seizures ceased while needle was still in vein. No seizures were noted following medication. Patient was discharged to ward within 3 days.

Case 6: E.H., male, age 48, I.Q. 75
Classification, Idiopathic - Undifferentiated
Onset of Epilepsy, 12 years of age
Predominant type of seizure, Grand Mal and Petit Mal
Physical Status, Pulmonary Tuberculosis - arrested

He was admitted to the hospital at 11:00 a. m., December 27, 1946 because of a series of rapidly repeated seizures which began at 10:00 a. m. He previously had severe repeated serial seizures of alarming nature following which he developed pulmonary edema, confusion and almost died.

He was given Sodium Delvinal (0.3 G) intramuscularly at 11:20 a. m. No seizures were recorded following medication and no further serial seizures were noted during the period of observation in the hospital which lasted about 2 weeks.

Case 7: I.H., female, age 26, I.Q. 98
Classification, Idiopathic - Undifferentiated
Onset of Epilepsy, 15 years of age
Predominant type of seizure, Grand Mal
Physical Status, This patient was admitted to the hospital on August 30, 1946 with a fracture of the left fibula

At 9:00 a.m. on December 28, 1946 she manifested repeated serial seizures every 15 minutes since 8:00 a.m. Delvinal Sodium (0.3 G) was administered intramuscularly at 10:40 a.m. Seizures stopped immediately. No mental sequalae were noted.

On January 5, 1947 at 7:00 a.m. she developed continuous myoclonus. Sodium Delvinal (0.3 G) was given intramuscularly at 8:00 p.m. Myoclonus ceased shortly afterwards. This patient has received this medication on various other occasions for myoclonus and it has been effectual.

Case 8: E.J., male, age 19, I.Q. 50
Classification, Idiopathic
Onset of Epilepsy, 6 years of age
Predominant type of seizure, Grand Mal
Physical Status, Undernournished and weak

This patient was admitted to the hospital on December 29, 1946 at 8:00 a.m. following series of rapidly repeated seizures of 3 hours duration. He was given a special bromide mixture (60 grains) orally but seizures continued.

At 2:45 p.m. he was given sodium luminal (1.0 G) intramuscularly. Seizures continued. Patient was weak, general condition poor and incipient pulmonary edema developed. Blood pressure at 5:30 before medication 140/118. Patient was given Delvinal Sodium (0.6 G) intramuscularly at 5:35 p.m. Blood pressure at 6:00 p.m. was 120/96. No further seizures were observed after 6:00 p.m. and physical condition improved rapidly. Pulmonary edema disappeared. Patient was discharged to his ward within 3 days.

Case 9: J.J., male, age 19, I.Q. 58
Classification, Symptomatic due to birth injury
Onset of Epilepsy, 7 years of age
Predominant type of seizure, Grand Mal
Physical Status, Genu Valgum. Athetoid movements of hands. Weight 90 lbs., emaciated.

This patient was treated in ward at Colony infirmary for rapidly repeated serial seizures which began at 4:00 a.m. on January 22, 1947. He was given an S.S. enema and triple bromide mixture (120 grains) by rectum. Seizures stopped at 5:00 a.m.

At 7:30 a.m., serial seizures were resumed at 15 minute intervals. Sodium Phenobarbital (0.6 G) administered intramuscularly was ineffectual. The medication was repeated at 9:45 a.m.

The seizures continued at the same rate and his respirations were shallow and his pulse weak (T 97.6, P 130, R 30). He was given Delvinal Sodium (0.3 G) intravenously at 10:50 a.m. The seizures stopped almost immediately and the patient slept till the next morning.

Pulmonary edema developed and at 8:00 p.m. on January 23rd his temperature was 105.2; pulse was 160 and respiration 44.

On January 24th he had one grand mal seizure at 1:00 a.m. He had grand mal seizures hourly from 7:00 a.m. to 10:00 a.m. He had Delvinal Sodium (0.3 G) intramuscularly and the seizures stopped. His temperature was 99.6, pulse 92, respiration 24. The pulmonary edema disappeared. No seizures were noted until 8:00 p.m. on January 28th when he had 1 grand mal seizure.

In addition to his serial seizures, this patient developed an abscess of his left hand and severe decubitus of buttocks.

On January 29th, he definitely developed acute cattarhal jaundice which was endemic at the institution at that time. Despite these complications, the patient was noted early in February as showing improvement mentally and physically. He only had 3 grand mal seizures on January 29th and January 30th and no mental sequalae were observed. However, the patient continued in a weakened condition for some time as a result of the above mentioned complications. No further serial seizures were noted.

Case 10: M.G., male, age 21, I.Q. 64
Classification, Idiopathic
Onset of Epilepsy, 3 years of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Negative

He was admitted to the hospital from his cottage dormitory at 3:05 p.m. on February 9, 1947 following 4 severe grand mal seizures in 30 minutes. He was given Sodium Delvinal (0.6 G) intramuscularly at 3:05 p.m. No seizures were noted following medication and no mental sequalae were present. He was discharged from the hospital on February 10, 1947 in good condition.

II. *Status Epilepticus*

Case 11: M.S., female, age 32, I.Q. 100
Classification, Symptomatic epilepsy associated with Pernicious Anemia
Onset of Epilepsy, 16 years of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Pernicious Anemia

While under treatment at the hospital for pernicious enemia on May 28, 1946, she developed status epilepticus at 11:15 p.m. She was given sodium luminal (0.3 G) intramuscularly at 11:30 p.m. and sodium amytal (1.0 G) intravenously at 11:50 p.m. but the severe status continued and the patient appeared in extremis.

On May 29, 1946 at 1:30 a.m. she was given Sodium Delvinal (0.6 G) intravenously. This was immediately effectual. No seizures were noted following medication. She slept until 8:00 a.m. The slight confusion which ensued disappeared by noon on May 29th.

Case 12: F.K., female, age 30, I.Q. 100
Classification, Idiopathic
Onset of Epilepsy, 17 years of age
Predominant type of seizure, Grand Mal
Physical Status, Negative

This patient was admitted to Colony hospital from her cottage on June 25, 1946 at 2:00 p.m. because of status epilepticus of 12 hours dura-

tion. Routine measures had failed to effect the seizure manifestations. At 3:05 p. m. she was given Delvinal Sodium (0.3 G) intravenously. The status epilepticus disappeared while the needle was still in the vein.

However, the next day the patient developed myoclonic attacks daily which responded to Sodium Delvinal (0.3 G) intravenously. She continued to have frequent myoclonic attacks daily for one month which appeared to be of psychogenically superimposed origin. She was discharged from the hospital on August 7, 1946 after psychotherapy and Sodium Delvinal orally had diminished the myoclonus.

Case 13: R.K., female, age 47, I.Q. 90
Classification, Symptomatic (meningo-encephalitis)
Onset of Epilepsy, 13 years of age
Predominant type of seizure, Grand Mal
Physical Status, Deep reflexes increased. Weight 105 lbs.

This patient was admitted to the hospital on August 13, 1946 at 8:00 p. m. with status epilepticus of one day's duration. The status responded immediately to 0.3 G of Sodium Delvinal intravenously.

On August 19, 1946 she had 7 grand mal seizures from 7:00 a. m. to 10:00 a. m. At 10:45 a. m. Delvinal Sodium (0.3 G) intravenously was given. There were no seizures until 7:00 p. m. She then had a series of 25 grand mal seizures within 1 hour. Delvinal Sodium (0.3 G) intravenously at 8:00 p. m. was given. Seizures ceased immediately.

On August 29, 1946 she developed severe myoclonus followed by status epilepticus. At 12:35 a. m. she was given Delvinal Sodium (0.3 G) intravenously. No apparent effect was noted. At 12:45 a. m. 0.3 G was given again intravenously. She slept following this last dose and seizures ceased. No immediate psychologic after effects were noted. However, on September 2, 1946 she had severe myoclonus at 6:00 p. m. Sodium luminal (0.3 G) was given intramuscularly at 7:00 p. m. No apparent effect was observed. Delvinal Sodium (0.3 G) was administered intravenously at 8:00 p. m. It was effectual. She slept thereafter until 6:00 a. m.

On September 6, 1946 she had severe myoclonus. Delvinal Sodium (0.6 G) intravenously was administered. The myoclonus ceased. She was discharged from the hospital October 7, 1946. No further seizures or myoclonic reactions were noted.

Case 14: D.H., male, age 7, I.Q. 7
Classification, Symptomatic (Aenesis)
Onset of Epilepsy, 6 months of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Left internal strabismus. Blindness of left eye; he cannot stand or walk.

This patient was admitted to the hospital on September 14, 1946 at 8:30 a. m. Patient brought from children's infirmary ward having had status since 6:00 a. m. He failed to respond to routine measures. He was given Delvinal Sodium (0.3 G) intravenously at 8:45 a. m. Seizures ceased while needle was still in vein. No further seizures occurred and he was returned to the children's ward the next day.

Case 15: C.F., male, age 5, I.Q. 15
Classification, Symptomatic - Agenesis
Onset of Epilepsy, 10 months of age
Predominant type of seizure, Grand Mal
Physical Status, Skull and face asymetrical; hard palate high, narrow and irregular; spasticity of lower extremities.

He was admitted to the hospital infirmary ward on November 2, 1946. Patient had repeated continuous grand mal seizures every 10 minutes since 6:00 p. m. which developed into status epilepticus at 11:40 p. m. He failed to respond to routine measures. At 1:35 a. m. on November 3rd, he was given Delvinal Sodium (0.3 G) intravenously. Seizures stopped while needle was still in vein. No further seizures were observed.

Case 16: C.P., male, age 28, I.Q. 52
Classification, Symptomatic - Agenesis
Onset of Epilepsy, 12 years of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Lateral nystagmus. Spasticity of lower extremities.

This patient was admitted to the hospital on November 27, 1946 at 9:30 a. m. He had developed status epilepticus at 9:20 a. m. He was given sodium amytal (1.0 G) intravenously at 9:45 a. m. but the seizures continued. He was given Sodium Delvinal (0.3 G) intravenously at 11:00 a. m. Status epilepticus ceased at 11:05 a. m. and the patient fell asleep. No further seizures nor mental sequalae were noted. Patient was discharged from the hospital within 3 days.

Case 17: L.H., male, age 8, I.Q. 30
Classification, Symptomatic (Agenesis)
Onset of Epilepsy, 6 months of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Epicanthal folds present; right external strabismus; left lower extremity has contraeture of elbow, hand and wrist. Spastic paresis of left upper and lower extremities

This patient was admitted to the hospital on December 16, 1946 at 9:35 a. m. At 9:45 a. m. patient was put to bed and given routine treatment. Seizures continued and at 9:50 a. m. patient developed status epilepticus. At 11:05 a. m. he was given Delvinal Sodium (0.3 G) intravenously. Status discontinued at 11:13 a. m. No further seizures were observed.

Case 18: R.S., male, age 10, I.Q. 36
Classification, Symptomatic (Agenesis)
Onset of Epilepsy, 1½ years of age
Predominant type of seizures, Grand Mal
Physical Status, Patient is unable to walk and is incontinent. Hypotonia of all right extremities

This patient was admitted to the hospital ward on December 24, 1946 at 6:00 p. m. He had developed status epilepticus at 5:00 p. m. following a series of seizures which began at 2:00 p. m. After routine measures had failed, he was given Delvinal Sodium (0.3 G) intravenously at 8:00 p. m. The seizures ceased while needle was still in vein. He was restless for about 1 hour but fell asleep at 1:00 a. m. and slept till 7:00 a. m. December 25th. At 6:00 p. m. on December 24th, his temperature was 95.8; pulse 64; respiration 16. At 7:00 a. m. on December 25th, his temperature was 98.4; pulse 84; respiration 20.

No further seizures were noted. He at his regular diet and was returned to his ward on December 25, 1946 at 5:00 p. m.

Case 19: J.M.S., male, age 20, I.Q. 94
(Status preceding and following serial seizures)
Intramuscular and intravenous administration
Classification, Symptomatic (Traumatic)
Onset of Epilepsy, 15 years of age
Predominant type of seizure, Grand Mal
Physical Status, Severe aceiform scars due to bromidism; spastic paralysis of left lower extremity and paresis of right lower; left parietal flat operative scar. Pulmonary tuberculosis; surgical correction of Genu Valgus

On January 7, 1947 at 6:00 a. m. while a patient in the hospital, he developed status epilepticus. He was given Delvinal Sodium (0.6 G) intramuscularly, and the seizures stopped. On January 9, 1947 from 6:00 p. m. to 5:45 a. m. on January 10, he had a series of seizures. On January 10, 1947 at 5:45 a. m. he was given Delvinal Sodium (0.6 G) intramuscularly and the seizures ceased.

On January 14, 1947 patient had 5 grand mal seizures between 7:00 p. m. and 9:30 p. m. Seizures ceased after administration of (0.6 G) Sodium Delvinal intramuscularly at 9:30 p. m.

On January 15, 1947 between 12:30 p. m. and 1:00 a. m. patient had 5 grand mal seizures. From 7:10 a. m. to 8:40 a. m. he had 8 grand mal seizures. At 8:50 a. m. he was given Delvinal Sodium (0.3 G) intramuscularly. From 9:10 a. m. to 10:45 a. m. he had 5 grand mal seizures. Seizures ceased until 6:00 p. m.

On January 15, 1947 from 6:00 p. m. to 8:00 p. m. seizures developed again. He had Delvinal Sodium (0.6 G) intramuscularly. No seizures following medication.

On January 17, 1947 from 7:25 a. m. to 10:30 a. m. he had 7 grand mal seizures. At 10:35 a. m. he was given Delvinal Sodium (0.3 G) intramuscularly. Seizures ceased at 1:40 p. m. From 11:15 p. m. to 12:45 a. m. on January 18, 1947 patient had 9 grand mal seizures. He was given Delvinal Sodium (0.3 G) intramuscularly at 1:00 a. m. on January 18, 1947. On January 18, 1947 from 7:00 p. m. to 9:20 p. m. patient had 10 grand mal seizures. At 9:30 p. m. Delvinal Sodium (0.3 G) intramuscularly following which he had 12 grand mal seizures which appeared to be increasing in severity and on January 19, 1947 patient developed status epilepticus. He was given Delvinal Sodium (0.3 G) intravenously. No seizures were noted following medication.

On January 20, 1947 patient had approximately 10 serial seizures. He was given Delvinal Sodium intramuscularly following which he had 6 grand mal seizures. At 9:25 a. m. he was given Delvinal Sodium (0.3 G) intravenously. Patient slept soundly and the seizures stopped.

On January 21, 1947 from 12:15 a. m. to 1:50 a. m. he had 10 grand mal seizures. He was given Delvinal Sodium (0.3 G) intramuscularly. No seizures were noted following medication.

On January 22, 1947 from 4:00 p. m. to 6:45 p. m. he had 18 grand mal seizures. He was given Delvinal Sodium (0.3 G) intramuscularly at 6:45 p. m. From 6:45 p. m. to 8:00 p. m. following Delvinal Sodium medication he had 12 grand mal seizures. At 8:30 p. m. he was given Sodium Delvinal (0.3 G) intravenously. No seizures were observed for the remainder of the night. On January 25, 1947 he had 6 grand mal seizures between 12 midnight and 12:30 a. m. On January 26, 1947 he was given Delvinal Sodium (0.3 G) intravenously. No seizures occurred following last medication. He had neither serial seizures nor status again but did have severe grand mal seizures.

A tentative diagnosis of lung abscess had been made in January. Further study revealed that he had developed pulmonary tuberculosis and was transferred to the tuberculosis ward in February.

Case 20: G.H., female, age 22, I.Q. 90
(Status following and preceding serial seizures)
Intravenous administration
Classification, Endocrinopathic
Onset of Epilepsy, 12 years of age
Predominant type of seizure, Grand Mal and Petit Mal (mixed)
Physical Status, Pituitary obesity

This patient was admitted to the hospital at 7:00 a. m. on February 1, 1947 from the dormitory. Patient had 27 grand mal seizures from 11:05 p. m. on January 31, 1947 to 7:00 a. m. on February 1, 1947. She was given sodium luminal (0.3 G) at 1:50 a. m. and sodium amytal (1.0 G) intravenously at 7:00 a. m. She was given an enema and 60 grains of triple bromide preparation at 7:30 a. m. She was given medications (repeated) at 1:00 p. m. as she had 88 grand mal seizures between 7:00 a. m. and 4:30 p. m. At 4:30 p. m. she developed definite status epilepticus. She was given Sodium Delvinal (0.6 G) intravenously at 6:00 p. m. The status epilepticus was controlled for 2 hours. At 8:00 p. m. she again developed serial seizures and had 12 seizures between than and 7:00 a. m. on February 2, 1947. The dose of Delvinal Sodium was repeated but she had 4 grand mal seizures between 7:00 a. m. and 1:00 p. m. on February 2, 1947. At 1:05 p. m. she was given (0.3 G) of Sodium Delvinal intravenously and the seizures ceased. The patient was returned to her own ward within 3 days in good physical condition. No mental sequalae noted.

Three additional cases suffering from status epilepticus responded within an hour after the intravenous administration of Sodium Delvinal where other measures had previously failed.

Two additional cases of severe serial seizures which did not respond to Delvinal are discussed below:

a) B.B., a 48 year old imbecile was admitted to the hospital ward on January 13, 1947 at 7:00 p. m. He had fallen about two days prior to admission, sustained a severe contusion to his head, and was suspected by the ward physician of having sustained a fractured skull.

However, it was also ascertained later that since the time of the fall or possibly just before it, he had had a severe seizure and that serial seizures supervened. The exact time of their initial occurrence was not certain but for at least the last 24 hours the serial seizures had assumed alarming proportions and when admitted to the hospital they were observed to occur at 10 minute intervals. He was in a very critical physical condition. His respirations were shallow and rapid. The respiratory rate was 36.

Between 7:00 p. m. on January 13th and 7:00 a. m. January 14th he received 20 grains of phenobarbital sodium intramuscularly and 120 grains of a triple bromide mixture by rectum. He also received about 20 grains of chloral hydrate by the latter route.

From 7:00 a. m. January 14th until noon, the seizures occurred at hourly intervals. However at noon they became more frequent and occurred about every 15 minutes. At that time his respirations were shallow and were about 44 per minute. Pulmonary edema appeared to be present. His temperature was 102° F and the pulse rate 120. His pulse was thready and weak.

At 1:30 p. m. he was given (0.6 G) of Sodium Delvinal intramuscularly. The seizures ceased until 4:00 p. m. but his general condition was very poor. His blood pressure was 70/30, pulse rate 140 and his respirations 44.

From 4:00 p. m. to 8:30 p. m. he had nine grand mal seizures. At 8:30 p. m. he received (0.6 G) of Sodium Delvinal intravenously. The seizures stopped until 7:00 a. m. the next morning (January 15th) but he was in very poor general condition.

On January 15th, he had 8 grand mal seizures from 7:05 a. m. to 8:45 a. m. He was given (0.6 G) of Sodium Delvinal intramuscularly. He had 9 grand mal seizures from 8:45 a. m. to 9:20 a. m.

At 9:25 a. m. he was given Delvinal Sodium (0.6 G) intravenously. The seizures ceased. However, at 9:30 a. m. his temperature was 105° F, his pulse was thready and very weak. The rate was 160. His respiratory rate was 48. At 12:05 p. m. his temperature was 107.6° F and his pulse was imperceptible. He expired at 12:50 p. m.

Clinically, the cause of death was thought to be exhaustion following seizures and pulmonary edema. Autopsy revealed areas of hypogenesis of the brain which was smaller than normal and fatty infiltration of the heart muscle which was thin-walled as well. The pathologist ascribed the cause of death to myocardial degeneration.

Comment: In addition to the complicating factors, i.e., myocardial degeneration and cerebral agenesis, this case report illustrates the poor prognosis to be expected in one prolonged episode of serial seizures which lasted at least 24 hours before active measures to combat it were undertaken. Despite oft repeated admonitions, early manifestations of serial seizures are frequently missed, overlooked or taken too lightly particularly if the patient has recovered from them previously. The temporal relationship, the frequency, and the severity as well as the serious nature of 3 or 4 seizures occurring in rapid succession or 6 severe seizures occurring during a 24-hour period are often overlooked. This is particularly true if the first manifestation of the seizures are mild or petit mal like in character. Status epilepticus and serial seizures frequently follow withdrawal of anticonvulsive drugs and should be carefully watched for.

The administration of Sodium Delvinal or other adequately active measures did not prevent this man's demise, although his seizures were finally in some measure controlled. The importance of instituting active measures as early as possible cannot be stressed sufficiently.

b) R.W. is a case illustrating the poor prognosis in patients with repeated serial seizures of one month's duration prior to admission to hospital.

This 13-year old bedridden, emaciated male

with an I.Q. of 20 was admitted to the hospital from the children's ward set aside for helpless epileptic patients on June 28, 1946. He was suspected of having bacillary dysentery.

However, it was ascertained that he had manifested at least 6 seizures daily three or four times a week for approximately one month prior to admission to the hospital and that his physical condition had run a gradual down hill course. His weight was 45 pounds.

Following admission to the hospital he was observed to be in very poor physical condition and to have serial seizures every ten minutes for about 3 hours. He was given Delvinal Sodium (0.3 G) in divided doses at 10:30 a. m. and 10:50 a. m. on June 28th. He had one seizure at 19:40 a. m. The seizures ceased at 10:50 a. m. At 10:30 p. m. that evening he had one grand mal seizure.

On July 8th, he had 20 grand mal seizures between 7:00 a. m. and 10:00 p. m. The routine measures employed to combat them were uneffectual. At 10:00 p. m. he was given Sodium Delvinal (0.6 G) intravenously. No further serial seizures were observed till July 13th and 14th.

On July 13th and 14th, he experienced serial seizures which were again controlled by Sodium Delvinal (0.6 G) intravenously. From July 21st to July 27th, he had serial seizures daily which responded to Phenobarbital Sodium (0.3 G) intramuscularly.

On July 29, 1946, he developed status epilepticus. He was given Sodium Amytal (0.3 G) intravenously and Phenobarbital Sodium (0.3 G) intramuscularly. He failed to respond and died within 4 hours after the status epilepticus had developed. Permission for autopsy was denied.

Discussion of Results

I. *Status Epilepticus*

In the 10 consecutive cases of status epilepticus described in the case reports, cessation of seizures resulted in a relatively short period of time following the intravenous injection of Delvinal Sodium (0.3 G to 0.6 G). These patients were all closely observed at the hospital or hospital infirmary wards at Craig Colony as soon as possible after the inception of status epilepticus.

In general it appears best to inject 0.6 G as soon as possible after the seizures begin. However, in weakened or undernourished patients and in children particularly those who are underweight, it may be well to begin with 0.3 G and repeat the dose if necessary. Sodium Delvinal or other measures employed should be instituted as soon as possible after the status begins. The longer one waits the more grave the prognosis. Intramuscular injection (0.3 G to 0.6 G) given at the onset should always be supplemented by the intravenous administration of Delvinal Sodium as soon as the physician arrives.

Three other cases of status treated earlier in the study and not as carefully observed responded immediately to the intravenous injection of Delvinal Sodium (0.3 G). In two, measures employed previously had proved ineffectual. In the other, Sodium Delvinal was given in a very short period of time after the seizures began and the status was terminated immediately.

Post seizure mental sequalae such as psychomotor phenomena or confusion were reduced to a minimum. None of the cases of status showed any mental signs after a 12-hour period had elapsed. In only two, was there a slight period of mild confusion and in only one was this mild confusion present for approximately 10 to 12 hours.

The administration of Sodium Delvinal in many instances prevented the recurrence of status epilepticus or serial seizures which not infrequently occur following the initial manifestations although it did not do so in all cases. However, where these phenomena did recur, the manifestations were frequently milder and responded more easily to intravenous administration of Sodium Delvinal.

II. *Serial Seizures*

In 10 consecutive cases of serial seizures observed under the same careful conditions of observation as the patients with status, the same favorable results were obtained when (0.3 G to 0.6 G) or Sodium Delvinal was administered parenterally. Moreover, four of the 10 cases responded well to intramuscular injection of 0.6 G of the drug. The other six who received 0.3 G to 0.6 G of Delvinal Sodium intravenously responded almost immediately.

The advantage of the intramuscular ad-

ministration is that Sodium Delvinal can be given by the nurse very early in the course of, at the onset of the manifestations of serial seizures or as soon as the patient shows signs of impending serial seizures, i.e., two or more seizures occurring in rapid succession. In this way, subsequent attacks may be aborted or rapidly controlled. Another advantage is that intramuscular injection of Sodium Delvinal may be employed with more safety in patients who are in severely weakened condition.

When the intramuscular route is chosen, 0.6 G of Sodium Delvinal should be administered to obtain the most effective results except in children who are suffering from severe inanition or who are severely ill. A procedure which has yielded good results is to inject (0.6 G) of Sodium Delvinal intramuscularly as soon as serial seizures or status begin and to follow this within 30 minutes to an hour with intravenous injection of 0.3 G to 0.6 G of Sodium Delvinal.

However, in severe serial seizures as in status epilepticus, the administration of 0.6 G of Sodium Delvinal intravenously appears to be the most effective method of controlling the seizures. As with other barbiturates given intravenously or intramuscularly, it is advisable to begin with the larger or optimum dosage, rather than begin with smaller or divided doses and work up to the optimum or maximum doses.

As in status epilepticus, in many instances, Sodium Delvinal aborted the tendency of the serial seizures to recur soon after but it did not do so in all cases. This recurrence as well as the important factor of early administration are illustrated in the two who died following serial seizures and are not included in the 10 consecutive reports but were discussed in the 5 supplementary cases. In each case, while Sodium Delvinal controlled the individual episode of serial seizures, it did not prevent the occurrence of a subsequent group of serial seizures or status nor did it prevent the patients demise.

The first of these cases with a prolonged individual episode of serial seizures did not receive Sodium Delvinal until 36 hours had elapsed. In addition, he suffered from myocardial degeneration and cerebral agenesis. The recurrence of seizure was finally controlled but he died soon after.

The second of these cases also suffering from cerebral agenesis had repeated serial seizures for about one month prior to receiving Delvinal Sodium and repeated seizures for 5 weeks after. He did not receive Sodium Delvinal for 2 weeks prior to his death. Neither the intravenous nor the intramuscular injection of Sodium Delvinal prevented the occurrence of subsequent serial seizures although it did terminate the episode of an individual group of seizures.

These two cases illustrate the importance of the administration of the drug early in the course of serial seizures or status epilepticus and the danger of overlooking the serious nature of repeated seizures and their tendency to recur. Since status epilepticus is objectively a more alarming objective phenomena the serious nature of repeated seizures with intervals occurring in between may not be given the same attention as early as the case of status epilepticus. It should also be borne in mind as indicated in the consecutive case reports as well as the supplementary ones that serial seizures may eventuate into status epilepticus and that at times serial seizures may ensue after status epilepticus. In any event, serial seizures and status epilepticus have a tendency to recur in the same individual. Further, status and serial seizures frequently follow withdrawal of anticonvulsive drugs. As soon as seizures begin to increase, it is wise to inject Delvinal Sodium intramuscularly or intravenously to prevent these phenomena from occurring.

III. *Evaluation of Results*

1. Because of its rather rapid action, the intravenous injection of Delvinal Sodium more quickly and more effectively combatted the seizure phenomena encountered in status epilepticus and severe serial seizures than other means previously employed. Because of its low toxic effects, a wide margin of safety exists. The administration of 0.6 G or 10 grains produced practically no side effects. While 0.6 G was effective in terminating most of its seizures, it is felt that except in the very emaciated children, larger doses can and should be used if necessary without toxic effects. Since 0.6 G of Sodium Delvinal has proven as effective as 1.0 G of sodium amytal in controlling seizures and produces no marked hangover, it is recommended that

larger doses may be tried with a view to preventing the tendency for seizures to recur. Again, Sodium Delvinal may be repeated orally, intramuscularly or intravenously for several days though the serial seizures do not recur in order to prevent them. Because of the lower degree of tolerance developed by the average individual to Delvinal Sodium, the dosage can be more frequently repeated without diminishing the effect as much as some of the other barbiturates.

2. In serial seizures if given early enough in 0.6 G doses, Delvinal Sodium may be an effective method of combatting the milder types or aborting the appearance of the more severe types because of its fairly rapid action. It may be used as a preliminary to the intravenous method in status epilepticus or severe serial seizures. The intramuscular method may be used alone also in children with cachetic or toxic conditions or where one finds difficulty in injecting the drug intravenously.

3. While Delvinal Sodium administered intravenously proved superior to routine methods previously employed in controlling status epilepticus and serial seizures. The intravenous injection of sodium amytal had also proved very effective in causing cessation of these seizures.

The advantage of Sodium Delvinal as compared with sodium amytal in overcoming serial seizures and status are as follows: (a) Rapidity of effect. (b) Smaller dosage necessary to produce effect. (c) Lessened tendency for the mental or physical sequalae following status to occur. (d) Lessened degree of depth of narcosis produced but entirely adequate diminution of the motor phenomena. (e) Lessened tendency to paradoxic effects and excitement which sometimes follow barbiturate administration. (f) Development of lessened degree of tolerance.

4. The fact that practically no mental sequalae such as psychomotor or equivalent phenomena occurred is of itself important enough to indicate that Sodium Delvinal should be given serious consideration in controlling serial seizures or status epilepticus. In addition, the occurrence of physical sequalae such as pulmonary edema, exhaustion and respiratory embarrassment which make serial seizures and status difficult conditions to manage are considerably reduced by the use of Sodium Delvinal intravenously or intramuscularly. Finally, the death rate in seizures of the severity reported in this paper are usually about one in five or 20 per cent. In this group, only two of 25 or 8 per cent died.

5. It must be stressed that Delvinal Sodium should be given early in the course of the seizures to obtain maximum effects. The intravenous method is most effective but intramuscular injection of Sodium Delvinal if given early enough in milder seizures or if given in conjunction with the intravenous method is of considerable value particularly in weaker patients and children.

Summary

1. Delvinal Sodium Vinobarbital was administered intravenously and intramuscularly to twenty-five cases suffering from status epilepticus and severe serial seizures.

2. In 23 cases, the seizures were controlled, there was a minimum of post seizure mental or physical sequalae, and the patients responded very favorably.

3. Two cases in whom the serial seizures were prolonged before Delvinal Sodium was administered died, although the individual episodes of seizures were controlled.

4. Ten cases of serial seizures who received Delvinal Sodium intravenously and intramuscularly early during the course of the seizures and who were carefully observed from the inception of the seizures responded well.

5. In all 13 cases of status epilepticus who received Delvinal Sodium intravenously, the seizure phenomena were controlled.

6. Delvinal Sodium administered intravenously appeared to produce better results than measures previously employed in causing the cessation of serial seizures and status epilepticus.

7. Delvinal Sodium administered intramuscularly is of some value particularly in emaciated patients and children if given early enough during the course of serial seizures or if given in conjunction or prior to the intravenous method.

Post Mortem Findings in Prefrontal Lobotomy

(REPORT OF A CASE*)

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The surgical procedure, prefrontal lobotomy, was originated by Moniz in 1934 as an operation for certain types of insanity, particularly in those cases which show a marked forceful emotional reaction to the patient's ideas, delusional and otherwise. His work followed the experimental studies of Jacobsen in neurotic monkeys. Jacobsen was not only able to produce tension states in his experimental animals, but by removal of one or both frontal lobes was able also to relieve them so that frustration and tension no longer produced the intense upset that it did in the normal animal. Freeman and Watts have done much to popularize the procedure and have placed it on a sound surgical basis. It was felt that the operation upon the prefrontal white matter interrupted the large tract from the medial dorsal nucleus of the thalamus to the frontal lobe. The success of the operation no longer seems open to question, as many patients whose condition have necessitated institutional care for years have been so relieved that they not only are able to return home but also have been able to carry on very useful lives.

Because of the fact that with the exception of a small initial postoperative mortality these patients lived just as long as other individuals, there has been very little post mortem material available. For this reason, the studies of the brain of a case who died not postoperatively but five months following surgery might cast additional light on what actually occurred following the operation.

Because of the extensive work of Freeman and Watts in this field, the specimen in this case, after study at the Hermann Hospital, was sent to Dr. Freeman, and his pathological findings contribute significantly to this report.

Case Report

History: Mrs. L. J., a married, white woman 62 years of age, was admitted to the Hermann Hospital on August 6, 1941. The chief complaint as given by her family was that she had a marked personality change of twenty-one years' duration which necessitated constant custodial care in the home. They reported that for many years she had caused them great concern because of her mental changes and stated that it was impossible to have visitors in the home or to play the radio, and the neighbors frequently complained because the patient was noisy and screamed at night.

Psychiatric examination by Dr. A. Hauser showed that the patient was greatly concerned about two main obsessions which began in childhood: First, that she had taken some gun-powder when she was a child about ten years of age in the belief that it would make her menstruate; and, second, that at the age of 18 years she put a small amount of menstrual fluid in her boy friend's coffee, at the suggestion of a negro washwoman who told her that it would give her a steady boy friend with whom to go to church. She stated that she did not wish to marry the boy at that time, but later she fell in love with him and eventually married him. As a consequence of her two sins against the Lord, as she called them, she was being punished, along with her entire family. As punishment, she stated that her body had become different from that of other people, that she had no lungs, that her bones were getting larger, and that her flesh was ready to fall from her bones. She believed also that she had no heart and that a sack of pus was present in its place. She stated further that she could not die and must live forever to be punished for her sins. In spite of this, there were no suicidal ideas, but she was worried constantly and depressed because of the above mentioned factors.

Her past history, except for psychotic content, was irrelevant. She had had, however, radium treatment five years before for carcinoma of the cervix. There had been no serious illness except for her mental condi-

*From Hermann Hospital, Houston, Texas.

tion. The family history was negative for insanity.

The general physical examination showed her to be a thin woman, quite agitated, and her cooperation was difficult to obtain. She had glaucoma in both eyes, causing almost complete loss of vision except for perception of light. The neck, chest, and heart were normal except for a blood pressure of 170/90 and a soft mitral systolic murmur. There was an occasional extrasystole.

Dr. A. Hauser made the following note on August 7, 1941: The patient states that she had "no feeling." "It was done by someone else, and I did it for the sake of the church. They told me to take gun-powder. Then they told me to take a boy friend to church, and I gave him the blood (referring to menstrual fluid)." At this point she wept and cried. She thinks she has to stay on this earth eternally and be punished. "I never did intend to marry him, but the devil just stepped in my path and told me to do that (give him that blood). Others have to suffer for what I have done."

Diagnostic impression: Melancholia or depression with obsessive delusional ideas (not definitely suicidal).

Prior to operation she was continuously agitated, talked incessantly and frequently would curse by the hour. She hardly slept at all and kept other patients awake.

Operation August 7, 1941: Preoperative diagnosis—involutional psychosis; postoperative—same. Anesthetic: avertin and ether, plus novocaine. Operation: bilateral prefrontal lobotomy.

Procedure: Bilateral trephine openings were made 3 cms. back of the angle of the lateral orbit and 5 cms. above the zygoma in line of the coronal suture. The dura was opened and the prefrontal fibers were cut on both sides in line of the coronal suture, swinging from the level position down to the floor of the frontal fossa, and from that position up to the roof of the skull. A brain cannula previously introduced to a depth of the midline was used as a depth gauge. The depth of the cut was 5 cms. Her postoperative condition was good.

Follow-up notes made in the hospital were as follows:

August 8, 1941: Patient slept most of the day. She was roused occasionally and answered questions logically.

August 11, 1941: Sutures were removed and head rebandaged. Patient cursed most violently during the procedure.

August 13, 1941: Patient has been very quiet the past two days. She answers questions briefly, or will merely say, "I don't know." She does not want to do anything but lie in bed.

August 16, 1941: Patient has continued to be quiet, speaks when spoken to, and appears to be relatively normal except for the fact that she is confused about the identity of some of her relatives. The patient was discharged on this date.

* * *

Dr. Hauser presented this case before the Texas Neurological Society in November 1941. At that time, three months after operation, she was perfectly oriented and very pleasant, although at times she seemed to be unnecessarily so. There was no agitation whatsoever, although the family reported that twice she had cursed a little but had gotten over it very quickly. Since returning home she had been easy to handle and no longer was agitated. When asked specifically about those obsessions which had caused her so much trouble, she replied that they simply were ideas, but they did not bother her any more. For fifteen years, the family had not been able to have visitors without the patient becoming extremely agitated, but after the operation she not only was pleasant to company, but also seemed really to enjoy them. The family stated that they had had the first real Christmas with her in fifteen years and were very grateful for the operation.

On December 30, 1941, shortly after getting out of bed in the morning, she had a severe vomiting attack with pain in the chest, and died approximately two hours later. Post mortem examination was obtained.

Autopsy Report: The following notes were made from the autopsy report of Dr. Violet Keiller:

The body was embalmed before autopsy and was well done. Chest: No adhesions, very little edema, no old lesions.

Heart: Moderate increase in clear pericardial fluid, 50 cc. or less. Enormous dilatation of the right atrium, with corresponding thinning of the walls: all other chambers of the heart are greatly contracted. There

is no cardiac hypertrophy. The left ventricular wall is extremely contracted; and near the apex on its posterior surface there is an area of hyperemia with a few petechial hemorrhages. The diameter of this surface redness is 1½ cms. across and 3 cms. long. On gross section through this area, there is evidence of rather extensive old fibrosis spreading through the heart muscle, which is central rather than superficial. In the same area there is patchy recent ischemia, as indicated by white soft areas. There is no visible thrombosis in the vessel, but the branches here are very small and all the coronary vessels show calcareous beading with irregular narrowing of the lumen. The area of old fibrosis extends to involve the adjacent area of intraventricular septum. All valves are normal. Coronary orifices show some atheroma, but no narrowing; the aortic arch shows very slight atheroma; and below the arch there is not much evidence of this.

The remainder of the autopsy, except the brain, was negative, and there was no evidence of recurrence of carcinoma of the cervix. The cause of death was coronary thrombosis.

Pathological Studies

The report on the brain by Dr. Walter Freeman is as follows:

Specimen consists of entire brain, sectioned, received from Dr. James Greenwood, Jr., Hermann Hospital, Houston, Texas. A bilateral prefrontal lobotomy had been done. The brain was received in formalin.

Brain after Fixation: The brain was received and the pons and cerebellum removed and the cerebrum cut coronally back as far as the anterior part of the thalamus. Bilateral small incisions in each frontal cortex laterally were seen. These opened on each side into traumatized areas in the white matter which occupied most of the anterior thalamic radiation. At one point the genu of the corpus callosum was entered. The incisions in the white matter were in oblique plane corresponding to that of the coronal suture. Each of them entered the anterior horn of the lateral ventricle on each side. The incisions were quite clean, showing no gross evidence of hemorrhage. A large block for serial sections was taken to include the thalami.

LN 662 Lobotomy Brain: The brain appears unusually pale as though embalmed before autopsy; it is well fixed and well preserved regarding shape. There is scarcely a trace of atrophy of frontal poles. Blood vessels at base are atheromatous but there are no visible infarcts. Section through tip of genu opens the ventricle on the left and shows only a puncture wound in the white matter of the 3rd frontal convolution. (1) This same block about 10 mm. thick and running through the posterior portion of the genu, reveals a puncture wound of the genu and somewhat extensive traumatic cavitation deep in white matter sparing the entire superior frontal convolution and the fasciculus cinguli but sectioning the callosal fibers, those beneath the 2nd and 3rd frontal convolutions down as far as the opening of the sylvian fissure. (2) Below the cut impinges on the head of the caudate nucleus but does not damage it. (3) Coronal section through anterior, perforated space shows the maximum extent of the lesion on the left side. The instrument has entered the brain at the superior aspect of the 3rd frontal convolution and has undercut this, the 2nd, and the insular convolution (external capsule) in this region. The internal capsule seems to be untouched. The cut comes close to the cingulum as it curves around the genu, and there is a small puncture wound cutting across the base of the superior frontal gyrus. (3) 8 mm. back of this cut is the remainder of the incision, a scythe shaped lesion about 22 x 15 mm., principally beneath the middle frontal gyrus and injuring the cortex slightly at the base of the superior frontal sulcus. (4) There is no injury to the mesial surface to the fasciculus cinguli. (5) On the right side the lesion of the frontal lobe at the anterior tip of the genu is a fairly large, cystic area with damage to the cortex in the lateral portion of the orbital region. (1) 10 mm. posteriorly the lesion is fairly large, underlies the 2nd and 3rd frontal gyri, enters the ventricle, but does not impinge upon the caudate nucleus or the internal capsule. (2) At the anterior perforated space the lesion is larger but not as large as on the left side. The instrument has penetrated through the 3rd frontal convolution traumatizing the cortex slightly. (3) The callosal fibers are certainly involved; the 2nd frontal gyrus is undercut, and the 1st

and 3rd only partially. (4) At the level of the anterior perforated space the lesion is triangular and is limited to the white matter of the 2nd frontal convolution, entering a small fissure where the cortex dips down. (5) The ventricles are a little enlarged. There is a little enlargement of the sylvian fissure and sl. thickened vessels best observed opposite the optic chiasm. No abnormalities were observed elsewhere in the brain.

Photographs were taken of the specimen before the 2 thalami were dissected out for serial section.

Microscopic Examination: The interest in this case centers around the thalamus, which was embedded in celloidin and cut into serial sections, about forty of which were stained for myelin sheaths, and another forty for ganglion cells. The findings are clear-cut and unequivocal; the nucleus medialis dorsalis has undergone very extensive degeneration on both sides, but more so on the left. This degeneration is characterized by reduction in the number of ganglion cells, sometimes to as low as three to five per high power field, instead of the normal twenty to thirty. Furthermore, there is very definite proliferation of glia, many of the small cells being apparently in a stage of activity, as judged by their elongated shapes, and sometimes by the formation of rod cells. The individual ganglion cells do not show any particular characteristic change that would distinguish those remaining from the cells elsewhere in the thalamus, but there are occasional shadow cells, and occasional indications of neuronophagia. There is apparently no gross destruction, and probably only a moderate degree of shrinkage of the nucleus, although control material is lacking. The inner stratum of the nucleus dorsalis medialis has been preserved, and the other nuclei of the thalamus show no significant alterations.

The myelin sheath preparations are not entirely satisfactory. There seems to be a little less marked myelin sheath preservation in the nucleus medialis dorsalis than would be expected. Nevertheless, the vertical fibers weaving down toward the region of the hypothalamus seem to be quite well preserved, although they could not definitely be traced, and they probably are sweeping through the nucleus rather than originating in it.

The internal capsule and globus pallidus, which are on the same section, show no significant alterations. The blood vessels are moderately sclerosed, the choroid plexus and ependyma are substantially normal.

Comment: The pathologic findings in this case are clear-cut. The surgical lesions are clean and definite. They enter the ventricle on both sides, but apparently without traumatizing to any significant degree the cortex or the head of the caudate nucleus. The cavity formation is to be attributed, I believe, to the retraction of the tissues after sectioning of the axones, the contour of the brain being maintained owing to the significant integrity of the cortex, although how much atrophy had occurred in the frontal lobes cannot be told from this specimen, but much better from the employment of encephalography.

The findings in the thalamus are equally definite, consisting of some atrophy probably, and very definite disappearance of cells in the lateral portion of the large nucleus medialis dorsalis. This is the nucleus that in all probability projects to the frontal pole, and the cells have undergone retrograde degeneration without incurring any other significant pathologic alterations.

Summary and Conclusions

A case of involutional psychosis with marked obsessions, surgically treated by prefrontal lobotomy, has been reported. The death of this patient from coronary thrombosis five months postoperatively provided an excellent opportunity for pathological studies following the surgical procedure. From these studies there seems to be considerable evidence that atrophy of the nucleus medialis dorsalis of the thalamus followed the operation. This supports the theory that section of the fibers between the thalamus and the frontal lobes prevents emotional reaction to delusional or obsessional ideas.

A Mixed Medulloblastoma and Spongioblastoma of the Cerebellum with Spread to the Cerebrum and Spinal Cord*

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The propensity of gliomas, particularly medulloblastomas, to spread from their primary site to other parts of the central nervour system, is well recognized. Ollivier (1837) reported a case that Bailey and Cushing (1925) thought was a medulloblastoma, but which Ford and Firor (1924) considered to be one of sarcomatosis of the meninges. Spiller (1907) reported an ependymoma that extended from the fourth ventricle to the sixth cervical segment.

Earlier, there was great difficulty in differentiating between meningeal sarcomas and gliomas. Collier (1904) referred to an unmistakable case of spreading glioma as a fibro-sarcoma of the cerebellum. Ford and Firor (1924) described four sarcomas and added twenty-eight from the literature. These authors, Firor and Ford (1924) also described a case of meningeal gliomatosis. Bailey and Cushing (1926) concluded that cells formerly interpreted as sarcomatous were really glial and that meningeal sarcomata were extremely rare.

The establishment of the medulloblastoma as a distinct pathological entity, and its specific designation by that name is based on the studies of Bailey and Cushing (1925-1926). These authors point out that in nearly all medulloblastomas numerous spongioblasts are present and there may be scattered neuroblasts. The medulloblasts were considered as bipotential and representative of an antecedent stage of development. Cushing (1930) reviewed the entire problem of medulloblastomas in great detail.

While the tendency of medulloblastomas to spread in the central nervous system is well known, that other types of gliomas also spread is less well recognized outside neurologic circles. Cairns and Russell (1931) found among eight spreading gliomas, specimens of medulloblastoma, neuroepithelioma of retina, glioblastoma multiforme, astrocytoma and ependymoma. To these can be added a papilloma of the choroid plexus as reported by Van Wagenen (1930), and an oligodendroglioma as described by Cairns (1929). Winkelman and Eckel (1936) described three cases of medulloblastoma with extensive dissemination. Eden (1938) described a mixed-cell glioma of uncertain nature that spread throughout the entire subarachnoid space and into all of the ventricles. A similar extensive dissemination of a cerebellar ependymoblastoma was recently described by Tarlov and Davidoff (1946). Of 191 gliomas studied by these authors 68 were glioblastoma multiforme and in one of these cerebral implants were found. Among 58 astrocytomas, 15 oligodendrogliomas, and 6 mixed oligodendrogliomas and astrocytomas, no instances of dissemination were found. Among 11 ependymomas, implants were found in 3, one of which was of cerebral origin that had spread to the spinal cord. Another significant study is that of Polmeteer and Kernohan (1947) who reported 42 cases of meningeal gliomatosis, of which 20 were medulloblastoma, 6 glioblastoma multiforme, 5 ependymoma, 5 oligodendroglioma, 3 astrocytoma, 2 retinoblastoma and 1 pinealoma.

Spitz, Shenkin and Grant (1947), in a study of 97 medulloblastomas, found a relatively higher than usual incidence in adults, with a greater frequency of localization in the cerebral hemispheres in the adults, as compared to a cerebellar localization in children. This relationship of localization to age was also previously noted by Cushing (1930).

Case Report

E.P., a 35 year old, white, married male, born and reared in moderate circumstances, completed the eighth grade and joined the regular army at age 19 in 1929. Medical history was essentially negative until the onset of the present illness.

*From Section of Neurology, Winter Veterans Administration Hospital.

In March 1942, there was a gradual onset of episodes of morning nausea and vomiting, stumbling to the right, dizziness, right tinnitus, severe frontal and occipital headaches, numbness of the right side of the face, and personality changes manifested by "loss of initiative and ambition." These symptoms progressed until 6-10-42, when, upon admission to an Army station hospital, neurological examination revealed: ataxia, positive Romberg, hyperactive reflexes, and horizontal nystagmus. Spinal fluid was under normal pressure, and was chemically normal; the tap resulted in a four-day cessation of nausea and vomiting.

On 7-10-42 he had a sudden attack of stertorous breathing with periods of apnea. BP was 172/98. Pulse was slow and irregular, and a severe occipital headache was present. The latter was relieved by hyperextension of the neck and turning of the head to the left. Fundi showed bilateral papilledema. The patient was transferred to an Army general hospital on 7-11-42. On 7-13-42, he was transferred to Fitzsimmons General Hospital, where the neurological examination revealed: papilledema; retinal hemorrhages; horizontal nystagmus, more on left; paresthesias in distribution of the right trigeminal nerve; weakness of right lower face; diminished hearing on right, poor performance of coordination tests; no motor weakness of extremities; no rebound phenomenon; and normal reflexes. A right cerebellar tumor was suspected.

On 7-20-42, at operation, both cerebellar hemispheres were found tightly compressed in the posterior fossa. A large, extremely vascular, non-encapsulated tumor was found just to the left of the vermis. A large portion of it was removed by suction. The rim of the foramen magnum was removed for decompression. Microscopic study was reported as "sarcoma," composed of plump, mitotic, bipolar spindle cells, tending to pallisade around blood vessels.

Diagnosis: Polar Spongioblastoma.

Following a smooth post-operative course with loss of ataxia, he was given a thirty-day furlough on 8-21-42, but returned on 9-20-42, with occipital headache and vomiting. He was given x-ray therapy, 12,600 R units, with gradual disappearance of all symptoms and on 11-17-42 returned to limited duty, during which time he received 16,200 R units of therapy.

On 2-21-43 he was returned to the hospital at the request of his commanding officer because of "inability to carry out duties properly." Examination revealed lapses of memory, inability to concentrate, and minimal evidence of cerebellar dysfunction. On 4-9-43 he was given a medical discharge (CDD) from the Army.

For the next two years he worked successively as a civil service clerk, chicken farmer, and plumber's helper, with gradually decreasing economic effectiveness due to irritability, difficulty in thinking, occasional headaches, mild dizziness and ataxia.

On 6-1-45 he was admitted to a veterans hospital complaining of weight loss, nervousness, vomiting and headaches, and was found to have nystagmus, weakness of the right palate and some atrophy of the right optic nerve. He was transferred to Hines General Hospital, where he received more x-ray therapy in August 1945, with complete relief of symptoms, and was then discharged.

The patient worked as a plumber's helper until February 1946, when, in addition to vomiting, he first developed back pain, numbness from the waist down, loss of control of the left leg, ataxia to the left, and difficulty in starting urination. He was readmitted to Hines General Hospital on 3-12-46, where neurological examination revealed signs of a spinal cord lesion; and lumbar puncture revealed a complete subarachnoid block. He was given 9,600 R units to the spinal cord, and on 5-2-46 was found to have paraplegia with some spasticity, positive Babinski and Oppenheim reflexes, brisk knee and ankle jerks, sensory loss of pin prick as high as the 7th thoracic dermatome anteriorly, and a cord bladder. On 5-7-46 a laminectomy of T-3, 4 and 5 was performed, revealing "isolated areas of bulging" over the cord, and no extramedullary tumor. Following operation, the patient was given a course of x-ray, and he improved with some return of quadriceps motion. On 6-24-46 he was discharged, incontinent of urine and unable to walk.

On 8-7-46, because of his wife's inability to care for him further, he was admitted to Winter Veterans Administration Hospital.

Examination revealed neurogenic bladder

with urinary infection; spastic paraplegia with bilateral pyramidal tract signs; diminished to absent sensation in all modalities below the level of T-7, and diminished deep tendon reflexes in the upper extremities. Spinal fluid contained 620 mgm. per cent of total protein with 4+ globulin and 4 lymphocytes.

He was given a course of x-ray therapy over the spine. There was no essential change in symptoms until January 1947, when personality changes, characterized by increased aggressiveness and irritability, became marked. Multiple severe decubitus ulcer developed, along with increasing weight loss, weakness, and difficulty in swallowing, until his death on 5-13-47.

Post mortem examination: On removal of the brain and spinal cord in continum, the cerebrum was dry. The gyyri were flattened and the sulci narrow. The cerebral hemispheres showed no gross abnormalities. A soft, fungating cerebellar tumor was found on the right side. It involved the vermis, and appeared to arise from the latter. There was a defect in the infralateral part of the right cerebellar hemisphere, at which site some dura with black silk sutures was adherent. A wartlike mass projected from the left cerebellar hemisphere in the region of the tonsil. The medulla oblongata appeared broader than normal. In the spinal cord there were several places where the tumor presented itself on the surface. The most striking of these consisted of a soft, yellowish growth at the level of the fourth cervical segment on the right side. In the region of the mid-thoracic laminectomy, some extra-dural tissue was adherent to the cord. Intradural examination revealed some lumpy, yellow discoloration on the dorsal aspect of the cervical and thoracic region. In the lumbar region the dura was adherent to a nodular appearing spinal cord for a length of about six centimeters. The anterior surface of the spinal cord showed no abnormalities.

Serial sections through the cerebellum showed an area of tumor that was about 5.5 cm. in diameter involving all tissues. While it lay in the midline, it extended further into the right lobe than the left, inferiorally. The tumor tissue was circumscribed. Ventrally, it involved the floor of the fourth ventricle. The tumor was pink and spongy, with areas of hemorrhage in it. Posteriorlly the tumor reached the surface of the cerebellum and was adherent to the dura.

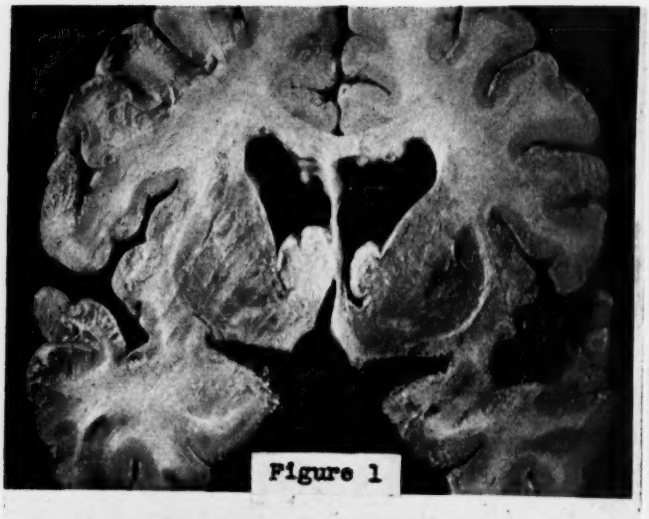
Serial sections of one-half inch thickness were also made coronally through the cerebrum. Ependymal nodules were present in the anterior horns (Fig. 1). These nodules involved the septum pellucidum as well as the other walls of the ventricles. There was mild dilatation of the ventricular system posteriorally. The posterior and inferior horns, as well as the third ventricle, were free of tumor tissue.

In a section through the middle of the medulla oblongata the floor of the fourth ventricle had a grey appearance. The degree to which the floor of the fourth ventricle was invaded by tumor is evident in Figure 2.

Spinal cord: At the junction of the medulla oblongata and cervical cord there was an elevation in the region of the cuneate and gracile tubercles. No gross abnormalities were noted in the middle of the cervical region, or at the cervico-thoracic junction. The upper thoracic segments showed some alterations in the dorsal columns, as did the lumbar spinal cord.

At the junction of the medulla oblongata and cervical cord tumor tissue replaced the right dorsal column. There was a smaller area invaded along the edge of the left lateral column, extending into the subarachnoid space. In the left dorsal column there was a less compact, diffuse infiltration of the cord. The blood vessels were plentiful, and congested with red blood cells. There was also considerable perivascular infiltration with tumor cells, as illustrated in Figure 4. Nerve cells were seen in various stages of degeneration.

The middle of the cervical spinal cord showed no tumor grossly, but some subarachnoid invasion by medulloblasts was evident microscopically in the region of the lateral columns. At the junction of the cervical and thoracic cord there was considerable subarachnoid infiltration which extended along the dorsal spinal roots, and into the dorsal horn region. While the dorsal root was surrounded by tumor tissue, it was not invaded. Here the tumor cells had a more uniform distribution and were less inclined to surround the blood vessels.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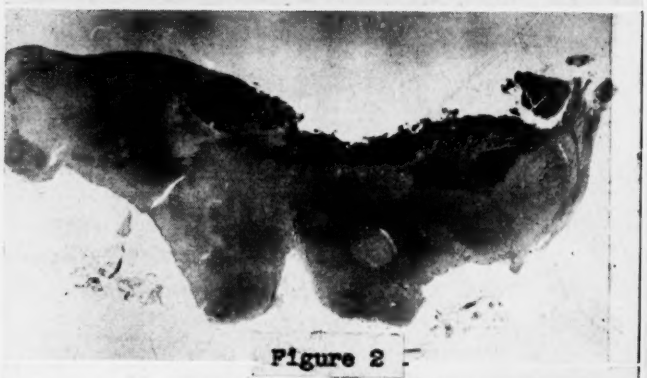
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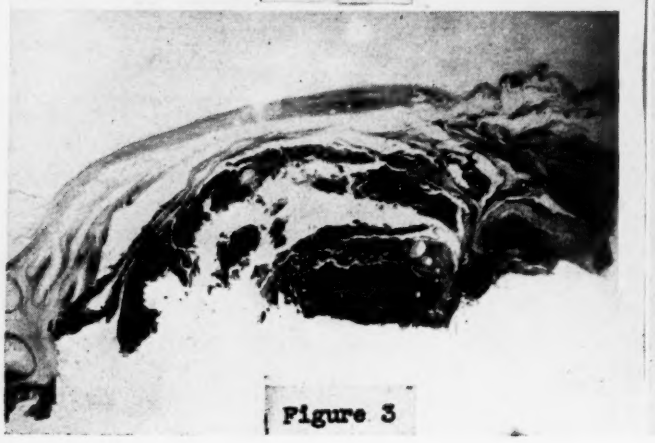
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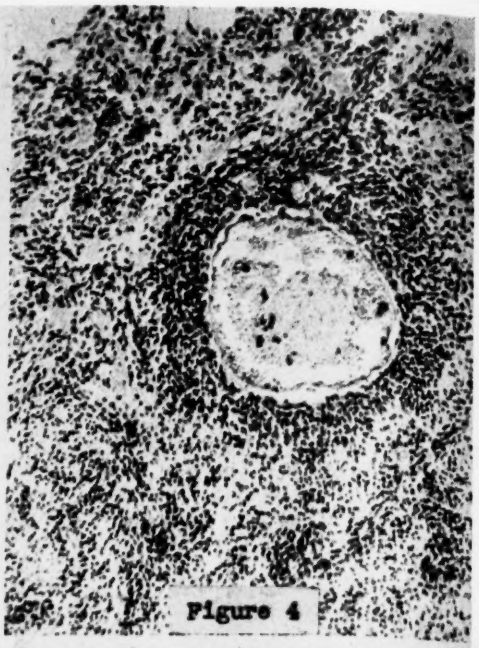
Figure 4

Figure 5

Figure 1: A frontal section through the anterior horns of the cerebrum illustrating the nodules of tumor tissue in the walls of the ventricles.

Figure 2: A section through the medulla oblongata showing the invasion of the floor of the fourth ventricle by tumor tissue. H and E stain.

Figure 3: This shows the heavy perivascular infiltration by medulloblasts that is present in some areas of tumor. H and E stain.

Figure 4: A section through the upper part of the thoracic spinal cord showing almost complete replacement of the latter by tumor tissue. The dura is not invaded. There is considerable subarachnoid and parenchymal hemorrhage in this region.

Figure 5: The spongioblasts are spindle-shaped and appear to stream through the medulloblasts among which they lie. H and E stain. High power magnification.

The upper dorsal cord (Fig. 3) was almost entirely replaced by tumor tissue. The dura was not invaded, however. At this level there was a moderate amount of subarachnoid hemorrhage and pigment laden phagocytes. The tumor cells in the subarachnoid mass were less uniform in size. In the spinal cord the tumor tissue was predominately medulloblastic, with some spongioblasts. Considerable hemorrhage was present.

At the level of the lumbar enlargement the posterior columns were invaded by tumor that was almost entirely medulloblastic. The extension of the tumor cells along the posterior roots and involvement of the posterior root ganglia was also evident here. Sections through the conus medullaris and cauda equina showed no tumor tissue, but there were degenerative changes in the anterior horn cells.

Microscopic study: These observations are based on H and E stained tissues. The tumor was highly cellular in nature, with two types of cells being present, medulloblasts and spongioblasts. The former were more common and consisted of small round or oval structures with scanty cytoplasm and a well defined, hyperchromatic nuclei. The nuclei were slightly irregular in shape and variable in size. In low magnification these cells appeared to be arranged in sheets, but on greater magnification they had no specific pattern but for pseudorosette arrangement here and there; and in some areas there was heavy perivascular infiltration (Fig. 4). In other areas, the cells lay in clumps, or were relatively uniformly distributed.

The spongioblast, which was less common, is a spindle-shaped cell with elongated nucleus, and scanty cytoplasm extending from both ends of the cell. They were so arranged as to give a streaming effect as they lay among the medulloblasts (Fig. 5). The spongioblasts were prominent in the tissue taken from the roof of the fourth ventricle, particularly in that derived from the lateral ventricles.

The cytological picture varied only slightly in the various parts of the nervous system. The tumor tissue in the right cerebellar hemisphere consisted entirely of medulloblasts, while the wart-like growth in the left cerebellar tonsil consisted of both spongioblasts and medulloblasts. The tumor nodules in the anterior horn of the lateral ventricle consisted of medulloblasts and spongioblasts. In the rostral end of the fourth ventricle there was increased vascularity, mitosis, and cellular anaplasia. The middle of the floor of the fourth ventricle contained many spongioblasts. In the fourth ventricle floor medulloblasts were arranged as pseudorosettes. Here the tumor tissue was quite clearly demarcated from the normal tissue. At the junction of the medulla oblongata and cervical cord, the increased vascularity of the tumor tissue was prominent. Neuroblasts, which may occur in medulloblastomas, were not found in the H and E stained tissue.

The blood vessels were abundant in the tumor tissue and consisted mostly of fine channels lying among the tumor cells and in the invaded neural tissue. They were mostly quite congested. Hemorrhagic areas were present (Fig. 3). Perivascular infiltration by tumor cells was marked in some areas (Fig. 4).

Discussion

In the light of the data presented in the introduction, it is of interest that the first biopsy tissue was diagnosed as sarcoma and polar spongioblastoma. Cairns and Russell (1931) describe a mixed medulloblastic and spongioblastic tumor with ventricular and spinal metastases. They also report a unipolar spongioblast of the third ventricle which spread to the spinal subarachnoid space below the 8th cervical segment. The variable nature of such tumors in different areas indicates the necessity of a complete study before a pathologic diagnosis is made.

Cairns and Russell (1931) call attention to the proliferation of meningeal capillaries which increased the blood supply of the tumor tissue in gliomatosis. Increased vascularity was prominent in the case described above.

The pathways followed by a spreading glioma appear to be several. There is invasion of adjacent areas of the nervous system merely by contiguity. When close to the subarachnoid space, the tumor may invade the latter and not only follow the flow of cerebrospinal fluid, but even spread against the latter. Otherwise, how could the lateral ventricle be invaded from the fourth ventricle? Cairns and Russell (1931), and Eden (1938) resort to the force of gravity in explaining

the spread to the ventricles as well as to the spinal subarachnoid space. They point out that the dorsal surface of the cord is more often involved than the ventral, in support of the gravitation theory. Winkelman and Eckel (1936) point out that post-operatively, the subarachnoid space may be invaded by particles of tumor deposited there by the operative intervention. Tarlov and Davidoff (1946) describe direct spread in the subarachnoid space by means of cerebrospinal fluid.

That gliomatosis also occurs over perivascular channels is discussed by Cairns and Russell (1931), and Winkelman and Eckels (1936). This is supported by the marked perivascular infiltration by tumor cells (Fig. 4), as seen in the case described. A similar distribution of cells is clearly illustrated by Winkelman and Eckels.

In our case, the spinal cord symptoms were prominent. Winkelman and Eckels (1936) report a case of spinal cord involvement that presented a picture of muscular dystrophy, with muscular wasting in the shoulder and gluteal regions, absent reflexes, and no sensory disturbance. On autopsy the spinal subarachnoid space was completely filled with tumor tissue and the periphery of the cord was invaded. All of the roots were imbedded in tumor. The spinal cord was almost completely destroyed. The authors were at a loss to explain the absence of sensory changes. The failure of root pain to develop, they surmised, was possibly due to the soft texture of the tumor tissue, which did not give rise to much pressure. Cairns and Russell (1931) state that in their cases spinal metastases gave rise to few or no signs, even when the cord was almost entirely surrounded by tumor. Collier's (1904) patient suffered extensive root pains, however. Eden (1938) described isolated palsies that cleared up, but was at a loss to explain these transitory phenomena. He also stressed the inconspicuous nature of meningeal signs, which one would expect to be quite prominent.

The treatment of medulloblastomas has become conservative. Bailey and Cushing (1925) advocated simple suboccipital decompression with subsequent x-ray therapy. Several series of x-ray treatments should be given over the cerebellum, ventricles, basilar cisterns and spinal cord following decompression. Cushing (1930) stressed the importance of the decompression because of the increased pressure that may follow irradiation. The radiosensitivity of this tumor is high, as described by Dyke and Davidoff (1942), and since operative intervention is liable to facilitate the seeding of tumor tissue into the subarachnoid space and thus hasten its spread, the avoidance of radical extirpation, and the adoption of Bailey and Cushing's therapeutic approach, has resulted in a better prognosis. Cushing (1930) pointed out that radical extirpation was associated with a high percentage of surgical fatalities.

Clinically it is evident from the course of the case described that x-ray therapy can afford relief for several years. This effect was formerly reported by Bailey and Cushing (1925), Winkelman and Eckel (1941), and Eden (1938). Bailey and Cushing (1925) refer to a case with what was then the longest symptom-free period, namely four years. This was between the first and second operations, during which four Roentgen treatments were given. In his splendid review, Cushing (1930) describes this case in a dramatic and very informative manner. Recently, Ingraham and Bailey (1944) reported survival in a case of medulloblastoma for nineteen years, and Penfield and Feindel (1947) published a case of medulloblastoma with a survival period of seventeen years. Spitz, Shenken and Grant (1947) found that the survival period was definitely longer in adults than in children.

Summary

A case of mixed cerebellar medulloblastoma and spongioblastoma with dissemination to the cerebrum and spinal cord is presented along with pathological studies. The pathogenesis, clinical diagnostic problems involved, and the treatment and prognosis of this condition are discussed.

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*The Localizing Value of Electrical Sign in Electroencephalography**

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A study of the electrical activity of the cortex and subcortex[1] in 24 patients with epilepsy by means of scalp electrodes and a multi-electrode needle, (placed in the depths of the brain with a stereotaxic instrument) indicates that if voltage measurements are referred to a relatively indifferent area, negative spikes on the cortex are commonly associated with positive spikes in the subcortex and vice versa. The same reversal of electrical signs is commonly observed on the cortex if recordings are made at a distance from a negative spike focus. It might be assumed that this reversal of sign is an artefact due to the use of a common reference electrode. This is not the case, however, for it is observed also with serial pairs of electrodes. The chief difficulty encountered with observing it with serial pairs of electrodes is that one or more pairs may be so oriented that they lie in an equi-potential line. Moreover, with serial pairs of electrodes electrical sign cannot be read directly but must be referred to the whole series of voltage readings.

The reversal of sign described here was noted by Dusser de Barenne and McCulloch[2,3] in their work with seizure potentials produced by local application of strychnine. They concluded that negative swings and negative spikes express activity originating in the area where the electrode is placed, with the nearest cell layers leading, whereas the positive swings with positive spikes indicate activity in more distant layers. They point out that their interpretation is in accord with the findings and interpretations of Bishop and collaborators,[4,5,6] or Marshall Woolsey and Bard,[7,8] and of Adrian.[9]

When isolated cortical spike or wave-and-spike pattern appeared the spike was almost invariably negative to a relatively indifferent area. Almost all subcortical discharges appeared as positive spikes which were associated with negative cortical spikes. On rare occasions, isolated subcortical negative spikes occurred independently of observed concomitant cortical spikes. Sharply localized posi-

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tive spikes were exceedingly rare; positive spiking tended to be diffuse.

Curtis' analysis[10] of potentials conducted through the corpus collosum also indicates that if an electrode is in the primary discharging area it will be driven negative with respect to a distant "indifferent" electrode, and positive if it is outside the primary discharging area or beyond the activated fiber system. The fact that *isolated* negative spikes were commonly found in the present study and isolated positive spikes exceedingly rarely, is in accord with Curtis' general conclusion that the primary disturbance is negative. He showed that an incoming volley from a fiber tract is picked up by a cortical electrode outside, and beyond the fiber system conducting the volley a positive potential is recorded, but this is usually followed by a secondary local response which appears as a negative disturbance. This local response can be increased by strychninization and decreased by the application of nembutal. Thus, a local response, even when secondarily initiated, is recorded as negative when referred to an indifferent area. The incoming fiber volley, however, is recorded as positive. It should be remembered that the positive "spread" of a local disturbance like a secondarily initiated negative spike results from nerve fiber conduction. It is not purely electrical or geometric; it is neuro-anatomical.

From the observations of other workers and the present findings it is possible to deduce a "law" which gives localizing value to the electrical sign in electroencephalography: *When electrical sign is referred to a relatively inactive area, negativity indicates a local disturbance; positivity indicates a distant disturbance.*

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NEWS NOTE

Residencies in Psychiatry are now available at the Veterans Administration Hospital, Gulfport, Mississippi. Training will be given at the Hospital and in New Orleans under the supervision of Tulane University and Louisiana State University Schools of Medicine. The program, approved by the American Medical Association and the American Board of Psychiatry and Neurology, will include didactic and clinical instruction in all phases of Psychiatry and basic Neurology, with experience in the techniques of treating Neuropsychiatric adults and children. Applications should be addressed to Dr. H. W. Kostmayer, Chairman of the Combined Deans' Committee, Tulane University School of Medicine, New Orleans, Louisiana.